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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
1644	9

DATE MAILED:

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 5/11/01

☑ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 51-59 is/are pending in the application.
Of the above, claim(s) 56,59 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 51-55,57,58 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

DETAILED ACTION

1. Applicant's amendment, filed 5/21/01 (Paper No. 8), is acknowledged.

Claims 50-55, 57 and 58 are under consideration in the instant application

Again, applicant's election of the species anti-CD28 antibodies in Paper No. 5, is acknowledged.

Again, claims 56 and 59 and the stimulatory form of a natural ligand of CD28 as the second agent have been withdrawn from consideration as being directed to a non-elected inventions/species. See 37 C.F.R. § 1.142(b) and M.P.E.P. § 821.03.

Claims 50-55, 57 and 58 are under consideration in the instant application.

Claim 1-49 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 5/21/01 (Paper No. 8).
The rejections of record can be found in the previous Office Action (Paper No. 6).

3. In response to the previous inquiry; applicant's amendment, filed 5/21/01 (Paper No. 8), asserts that USSN 08/253,964, filed 6/3/92, provides for the written description of the following claimed limitations.

(A) "a method for inducing ex vivo proliferation of a population of T cells";
(B) "covalently attached thereto";
C) "first and second agents";
D) "a stimulatory form of a natural ligand of CD28 (e.g. B7-1)" ;
E) "monitoring proliferation, reactivating and restimulating T cells"; and/or
F) "the recitation of claim 58".

4. Applicant is reminded to amend the first line of the specification to update the status of priority documents

5. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84.
Please see the form PTO-948 previously sent in Paper No. 6.
The Brief Description of the Drawings should be amended to recite the different part numbers of the drawings (e.g. Figures 5A-C).

6. Claims 50-55 and 57 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Thompson et al. (WO 90/05541) (1449, #A3) (see entire document) for the reasons of record set forth in Paper No. 6.

Applicant's arguments, filed 5/21/01 (Paper No. 8), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant argues that the prior art does not teach each and every element of the claimed invention, particularly, "a solid phase surface having covalently attached thereto a first agent and a second agent". In addition , applicant argues that the prior art indicates that there is no significant increase in T cell proliferation over that induced by anti-CD3 alone (see pages 2-3, overlapping paragraph).

However, in contrast to applicant's assertions, Thompson et al. does disclose the referenced method of immunotherapy with stimulated T cells can be used not only to increase T cell proliferation but to augment the immune response by increasing the levels and production of an entire set of T cell lymphokines (e.g.; see page 3, paragraph 1; page 6, paragraph 1 and Examples III-VIII).

It does not appear that the claim language or limitations do not result in a manipulative difference in the method steps when compared to the prior art disclosure.

Also, see Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999); Bristol-Myers Squibb Co. v. Ben Venue Laboratories Inc. 58 USPQ2d 1508 (CAFC 2001). See MPEP 2112.02.

It is noted that upon reconsideration of applicant's arguments, filed 5/21/01 (Paper No. 8); the previous rejection under 35 U.S.C. § 102(b) as being anticipated by Thompson et al. (WO 90/05541) would be withdrawn if the claimed methods are drawn to both the first agent and the second agent are covalently attached to solid phase and do not encompass methods wherein only the first agent must be covalently attached to a solid phase.

Thompson et al. (WO 90/05541) appears to teach the use of CD28-specific antibodies in solution and via cross-linking but does not appear to teach the use of immobilized CD28-specific antibodies per se as they would read on covalently attached CD28-specific antibodies.

7. Claims 50-55, 57 and 58 stand rejected under 35 U.S.C. § 103 as being unpatentable over Weiss et al. (J. Immunol. 137: 819-825, 1986; 1449, #E2) AND/OR Ledbetter et al. (J. Immunol. 135: 2331-2336, 1985; 1449, #B12) in view of the art known use of covalently linking antibodies to solid phase to deliver stimulatory signals to cells of interest, including T cells as well as the art known practice to monitor cell proliferation of interest, including cell size and cell markers at the time the invention was made for the reasons of record in Paper No. 6.

Applicant's arguments, filed 5/21/01 (Paper No. 8), have been fully considered but are not found convincing essentially for the reasons of record.

To some extent, applicant's arguments and the examiner's rebuttal are essentially the same as indicated above with respect as to whether both the first and second agent must be covalently attached to a solid phase surface.

In addition, as pointed out previously; given the art known use of applying immobilized antibodies to stimulate T cells, including the known use of anti-CD3 antibodies and multivalent forms /saturating amounts of anti-Tp44 (i.e. anti-CD28) antibodies to stimulate T cells, as taught by the teachings of Weiss et al. And Ledbetter et al.; one of ordinary skill in the art would have been motivated to stimulate antigen-specific T cells by covalently attaching both signals of anti-CD3 antibodies and anti-CD28 antibodies as a convenient and art known means to deliver said stimulatory signals to T cells ex vivo / in vitro. For example, it was known to provide such stimulatory signals by covalently linking the antibodies to plastic surfaces, as taught by Weiss et al. and Ledbetter et al. or via other convenient solid phase surfaces such as microbeads, as known and commercially available at the invention was made. It was readily understood and practiced by the ordinary artisan at the time the invention was made that by covalently linking such stimulatory agents to solid phase; the activated cells of interest would have been readily separated from the culture and agents and isolated accordingly.

Similarly, it was an art known practice to monitor cell proliferation of interest, including cell size and cell markers at the time the invention was made; as such criteria were known parameters of cell activation. Also, it was common practice at the time the invention was made to re-activate and re-stimulate cells to maintain proliferation and expansion of cell populations of interest at the time the invention was made.

Therefore, one of ordinary art at the time the invention was made would have expected to monitor the proliferation of said T cells by various parameters and to re-stimulate T cells undergoing expansion to achieve large number of cells of interest.

While applicant relies upon the inhibition by anti-CD45 antibodies disclosed in Ledbetter et al. (PNAS 85: 8628-8632, 1988: Appendix B); the claims are not drawn to anti-CD45 antibodies.

Clearly the prior art relies upon the effective stimulation of combining both anti-CD3 antibodies and anti-CD28 antibodies to stimulate T cells, including T cells for immunotherapy, as taught by Weiss et al. and Ledbetter et al.

Also, in contrast to applicant's assertions, both Weiss et al. and Ledbetter et al. teach that stimulating T cells by the combination of both anti-CD3 antibodies and anti-CD28 antibodies also results in increased proliferation as well as activation of T cells (e.g.; Ledbetter et al.; see page 3, paragraph 1; page 6, paragraph 1 and Examples III-VIII).

One of ordinary skill in the art at the time the invention was made would have been motivated to stimulate T cell activation with both CD3-/CD28-specific antibodies, including covalently linking both stimuli to solid phase surfaces, to increase T cell proliferation and numbers of T cells of interest for various purposes, such as T cell studies and adoptive immunotherapy. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary

Applicant's arguments are not found persuasive.

8. Claims 50-55, 57 and 58 stand rejected under 35 U.S.C. § 103 as being unpatentable over Weiss et al. (J. Immunol. 137: 819-825, 1986; 1449, #E2) AND/OR Ledbetter et al. (J. Immunol. 135: 2331-2336, 1985; 1449, #B12) in view of Zarling et al. (U.S. Patent No. 5,081,029) for the reasons set forth in Paper No. 6.

Applicant's arguments, filed 5/21/01 (Paper No. 8), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal are essentially the same as indicated above in Sections 6 and 7 with respect as to whether both the first and second agent must be covalently attached to a solid phase surface.

9. Claims 50-55, 57 and 58 are rejected under 35 U.S.C. § 103 as being unpatentable Thompson et al. (WO 90/05541) (1449, #A3) in view of the art known use of covalently linking antibodies to solid phase to deliver stimulatory signals to cells of interest, including T cells as well as the art known practice to monitor cell proliferation of interest, including cell size and cell markers at the time the invention was made for the reasons of record set forth in Paper No. 6.

Applicant's arguments, filed 5/21/01 (Paper No. 8), have been fully considered but are not found convincing essentially for the reasons of record.

In contrast to applicant's assertions, Thompson et al. does disclose the referenced method of immunotherapy with stimulated T cells can be used not only to increase T cell proliferation but to augment the immune response by increasing the levels and production of an entire set of T cell lymphokines (e.g.; see page 3, paragraph 1; page 6, paragraph 1 and Examples III-VIII).

Applicant's arguments are not found persuasive.

10. Upon reconsideration of the amended claims in copending USSN 09/183,055; the previous provisional rejection under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of commonly assigned copending USSN 09/183,055 have been withdrawn, as the claimed methods appear to be distinct from the instant methods. .

11. Claims 50-55, 57 and 58 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over
pending claims of commonly assigned copending USSN 08/403,253 and
pending claims of commonly assigned copending USSN 08/435,816

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant and copending claims appear to rely upon the same or nearly the same method steps and ingredients, particularly the use of anti-CD3 and anti-CD28 antibodies to stimulate and expand T cells.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

12. Given the common inventorship in commonly assigned copending USSN 08/403,253 and commonly assigned copending USSN 08/435,816; the issues under 35 U.S.C. § 102(f) or (g) appear to be obviated.

13. No claim is allowed.

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

PHILLIP GAMBEL

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